UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/582,679 | 05/17/2007 | Jo Klaveness | PN0397 | 7412 |

36335 7590 12/09/2008

GE HEALTHCARE, INC.
IP DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

| EXAMINER | |
|---|---|
| SCHLIENTZ, LEAH H | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1618 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 12/09/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/582,679 | KLAVENESS ET AL. | |
| | Examiner | Art Unit | |
| | Leah Schlientz | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

The information disclosure statement filed 6/14/06 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. In the instant case, copies of the foreign patent documents were not provided.

### *Claim Rejections - 35 USC § 101*

Claim 13 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an optical imaging contrast agent with an affinity for an abnormally expressed biological target associated with oesophageal cancer or Barrett's oesophagus of formula I, V-L-R, wherein V is one or more vector moieties having affinity for an abnormally expressed target in oesophageal cancer or Barrett's oesophagus, L is a linker moiety or a bond and R is one or more reporter moieties detectable in in vivo optical imaging, and wherein the contrast agent has a molecular weight below 10000 Daltons. However, the claims are devoid of any structural elements that correlate to the function which is to be achieved with the claimed composition. For example, a vast number of potential "vector moieties having an affinity for an abnormally expressed target in oesophagael cancer or Barrett's oesophagus" may be found in the art to be capable of having the claimed function. Applicant has identified in the instant specification a diverse variety of targets for which the vector may have affinity including VEGF, cytokines, endothelin, cox-2, cd44, etc. (see paragraphs 0026-0048 of the instant specification). Such targets are widely varying in structure and would have an almost unlimited number of potential vectors which may have affinity thereto. The vectors themselves may be almost unlimited including various pepdide sequences,

small molecules, antibodies, nucleic acid sequences, etc. It is clear that Applicant had possession of such a few specific formulations at the time of filing using specific and defined vectors as identified in paragraphs 0061-0066 and the Examples, but the specification as originally filed does not provide support that Applicant had possession of the invention as generically claimed by function alone in the instant claims. For example, to arrive at the claimed contrast agent, one would have to determine the type of vector having affinity to which out of an extremely large number of targets to conjugate to which out of an almost unlimited number of potential optical imaging moieties to be combined into a single agent, and further which out of an almost unlimited number of potential functional groups or chemical reactions would be necessary to derivatize and conjugate the moieties into a single agent having the claimed functional properties. One would have to select which portions of which molecules would be suitable to be conjugated to the others and on what positions of the molecules with various substituents. Applicant's limited disclosure of a particular compound which has the claimed functional properties does not provide support that Applicant envisaged the invention as a whole which is broadly claimed solely by function. In the instant case, a definition by function alone does not appear to sufficiently describe the claimed invention because it is only an indication of what the agent does, rather than what it is. See MPEP 2163 and *Eli Lilly,* 119 F.3 at 1568, 43 USPQ2d at 1406.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Weissleder *et al.* (US 2003/0044353).

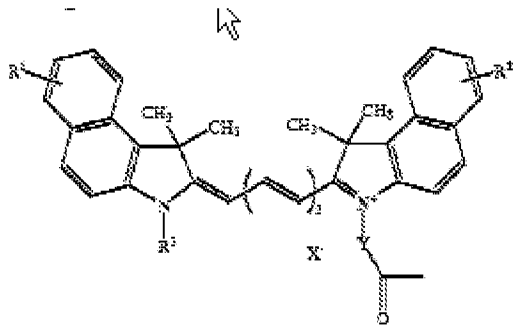
Weissleder discloses activatable imaging probes that includes a chromophore attachment moiety and one or more chromophores, such as near-infrared chromophores, chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of the plurality of chromophores are altered. The probe optionally includes protective chains or chromophore spacers, or both. Also disclosed are methods of using the imaging probes for optical imaging (see abstract). A number of specific peptide substrates including cathepsin B-specific peptide substrates, MMP substrates, thrombin substrates and others are included in the probes of the present invention (see, e.g., Table 2). Examples of cathepsin B-specific substrates include RRK(FITC)C-$NH_2$, etc. An example of a MMP substrate is Gly-Pro-Leu-Gly-Val-Arg-Gly-Lys(FI- TC)-Cys-$NH_2$) (paragraph 0089). Cathepsin D is also disclosed as a target. Spacers containing the amino acid sequence recognized by cathepsin D can be used to produce an imaging probe that undergoes activation specifically in breast cancer tissue. An example of a cathepsin D-sensitive spacer is the oligopeptide: Gly-Pro-Ile-Cys-Phe-Phe-Arg-Leu-G- ly (SEQ ID NO:1). Exemplary

chromophores include cyanines (cy5.5, cy5, cy7) (Table 1 and Examples). Pharmaceutical compositions include sterile injectable solutions including isotonic saline, etc. (paragraph 0128-0129). See also Examples.

Regarding the limitation of the instant claims wherein the optical contrast agent has an "affinity for an abnormally expressed biological target associated with oesophageal cancer or Barrett's oesophagus," it is noted that cathepsin D is associated with oesophageal cancer or Barrett's oesophagus, as evidenced by Applicant's specification at paragraph 0014. The intended use of the vector as "having affinity for an abnormally expressed target in affinity for an abnormally expressed biological target associated with oesophageal cancer or Barrett's oesophagus" has not been given patentable weight to distinguish over Weissleder because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Weissleder discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claims 1, 3, 5 and 7-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Ito et al. (US 5,968,479).

Ito discloses a diagnostic marker containing (a) a detection system such as an antibody and (b) a fluorescent functional group that is bound to the detection system and represented by the formula:



The diagnostic marker emits fluorescence having a wavelength of 780 nm or more when irradiated with near or far infrared rays, and thus useful for infrared endoscopic diagnosis or identification of a focus in surgical operation (abstract). Targeting to p53 protein for *in vitro* and *in vivo* targeting of cancer of the esophagus are disclosed (column 9, lines 10-30). See also Example 12. As pharmacologically and pharmaceutically acceptable additives for the manufacture of the diagnostic agent of the present invention, for example, excipients, disintegrators, etc. (column 11, lines 23+).

Claims 1-3, 6-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Klaveness *et al*. (US 6,610,269).

Klaveness discloses compositions of the formula V-L-R, where V is a vector moiety having affinity for an angiogenesis-related endothelial cell receptor, L is a linker moiety or a bond and R is a detectable moiety, characterized in that V is a non-peptidic

organic group, or V is peptidic and R is a macromolecular or particulate species providing a multiplicity of labels detectable in in vivo imaging (abstract). Particularly preferred vectors include amino acid derivatives such as described in WO94/02446, hydroxamic acid derivatives such as described in WO94/02447, thiazolopyrimidines such as described in EP-A-618208, triazoles such as described in WO95/08327, quinazolines such as described in WO97/30035, isoindolones such as described in WO97/37655, integrin inhibitors, VEGF antagonists, bFGF antagonists, thrombospondin and thrombospondin fragments, CD36 and growth factors (e.g. VEGF, bFGF, etc) (column 23). Preferred reporters include chromophores/fluorophores (e.g. cyanines, etc.) (column 42). See also Examples. Excipients are disclosed.

Regarding the limitation of the instant claims wherein the optical contrast agent has an "affinity for an abnormally expressed biological target associated with oesophageal cancer or Barrett's oesophagus," it is noted that VEGF receptor is associated with oesophageal cancer or Barrett's oesophagus, as evidenced by Applicant's specification at paragraph 0028. The intended use of the vector as "having affinity for an abnormally expressed target in affinity for an abnormally expressed biological target associated with oesophageal cancer or Barrett's oesophagus" has not been given patentable weight to distinguish over Klavenss because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136

USPQ 458, 459 (CCPA 1963). Since Klaveness discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/573,604, 10/573,606, 10/582,680, 10/582,842, and 10/582,893. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to an optical contrast agent with an affinity for an abnormally expressed biological target associated with oesophageal cancer of

formula V-L-R, wherein V is one or more vector moieties having affinity for abnormally expressed target in oesophageal cancer. The claims of the ‘604, ‘606, '680, '842 and '893 applications are drawn to optical contrast agents having formula V-L-R, wherein V has an affinity for abnormally expressed targets associated with endometriosis, colorectal cancer, atherosclerotic plaque, prostate cancer, and lung cancer, respectively. The specifications of the instant application and those of the '604, ‘606, '680, '842 and '893 applications, the vectors having affinity for various abnormally expressed biological targets may be the same (e.g. vectors for angiogenesis targets, adhesion molecules, estrogen receptors, metalloproteinases, e-cadherin, cathepsin B, cox-2, etc.). The contrast agents are the same and should be capable of the same functions. Accordingly the claims are overlapping in scope and are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

## ***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS